Utah Diabetes Practice Recommendations

Hyperglycemia Management for Inpatients

Section 3 in a series of topics included in the
Utah Diabetes Practice Recommendations
Updated April 2009

Diabetes Prevention
& Control Program
UTAH DEPARTMENT OF HEALTH

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Hyperglycemia Management for Inpatients

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Dissemination and Review

This section of the Utah Diabetes Practice Recommendations – Hyperglycemia Management for Inpatients, will be distributed to the medical and nursing staff, and the administration at major Utah area hospitals. It is recognized that the target glycemic levels included in these Recommendations, while based on current literature and expert opinion, are still the subject of professional debate.

We anticipate that future studies will potentially reduce or increase the appropriate levels of glucose control in hospitalized patients. In promulgating these Recommendations, we recognize that while they outline a general course of action for the majority of patients who experience hyperglycemia while in the hospital, they do not substitute for clinical judgment concerning the course of treatment for individual patients.

Diabetes and Hyperglycemia Management for Inpatients

INTRODUCTION

Background

Individuals with diabetes have significantly higher hospital admission rates, particularly for conditions related to coronary artery, cerebrovascular and peripheral vascular disease, and infections, nephropathy and lower-extremity amputations. In addition, a recent retrospective review of adult admissions suggested that nearly one-third of patients found to have hyperglycemia during hospitalization did not have a prior diagnosis of diabetes. Despite this, these patients were more likely to be admitted to the ICU, have longer hospitalizations and higher mortality compared to patients with known diabetes. Evidence is mounting from recent studies that hyperglycemia in the hospital may have serious consequences, and that morbidity and mortality can be reduced through aggressive treatment of hyperglycemia. Unfortunately, the management of the diabetes is considered secondary to the primary cause of admission, and in patients without a prior diagnosis of diabetes, hyperglycemia is frequently left untreated.

The purpose of this section of the Utah Diabetes Practice Recommendations is to provide insight and management protocols for hyperglycemic screening, treatment and achievement of glycemic targets. It is important to recognize that hyperglycemia occurs in three classes of patients:

- Patients with previously diagnosed diabetes known to the treating physician
- Patients with unrecognized diabetes (fasting blood glucose >126 or random blood glucose >200) during hospitalization and confirmed as diabetes after discharge, but unknown initially by the treating physician)
- Stress hyperglycemia secondary to severe illness occurring during the hospital stay that reverts to normal after discharge

The prevalence of diagnosed diabetes in hospital patients in Utah is reported to be 8.9% based on hospital discharge data, with only 9.8% of these having a principal diagnosis of diabetes. National experts estimate that the true prevalence of diabetes among hospital patients may be underestimated by as much as 40%.

Increased Morbidity and Mortality Related to Hyperglycemia

Several observational studies suggest an association between hyperglycemia and adverse outcomes. In one study involving patients undergoing general surgery procedures, postoperative complications (wound infections, sepsis and pneumonia) were 5.7 times more likely to occur in patients whose blood glucose exceeded 220 mg/dl. In a second study of 1,886 patients admitted to a general medicine service, 495 had known diabetes and 223 had “new” hyperglycemia. The new hyperglycemic cohort was likely composed of patients with unrecognized diabetes, prediabetes, and/or stress hyperglycemia secondary to severe illness. After adjusting for confounding factors, patients with new hyperglycemia had an 18-fold increase in hospital mortality and patients with known diabetes had a 2.7-fold increase in mortality compared with the normoglycemic cohort.

These data suggest that hyperglycemia from any etiology in the hospital on general medicine and surgery services is a significant predictor of poor outcomes relative to outcomes for patients who do not develop hyperglycemia. A third study evaluated the hospital care rendered to hyperglycemic individuals who did not have a diabetes diagnosis prior to admission. One third of hyperglycemic surgical patients did not have a diabetes diagnosis at the time of admission even though they had an average peak glucose of 299 mg/dl. While 54% of them received insulin therapy and 59% received bedside glucose monitoring, 66% of daily patient progress notes failed to comment on the presence of hyperglycemia or diabetes. Diabetes was documented in only three patients as a possible diagnosis in daily progress notes. Given the average delay of almost a decade between the onset and diagnosis of type 2 diabetes, further evaluation of hyperglycemia among hospitalized patients presents an important opportunity for earlier detection and treatment.

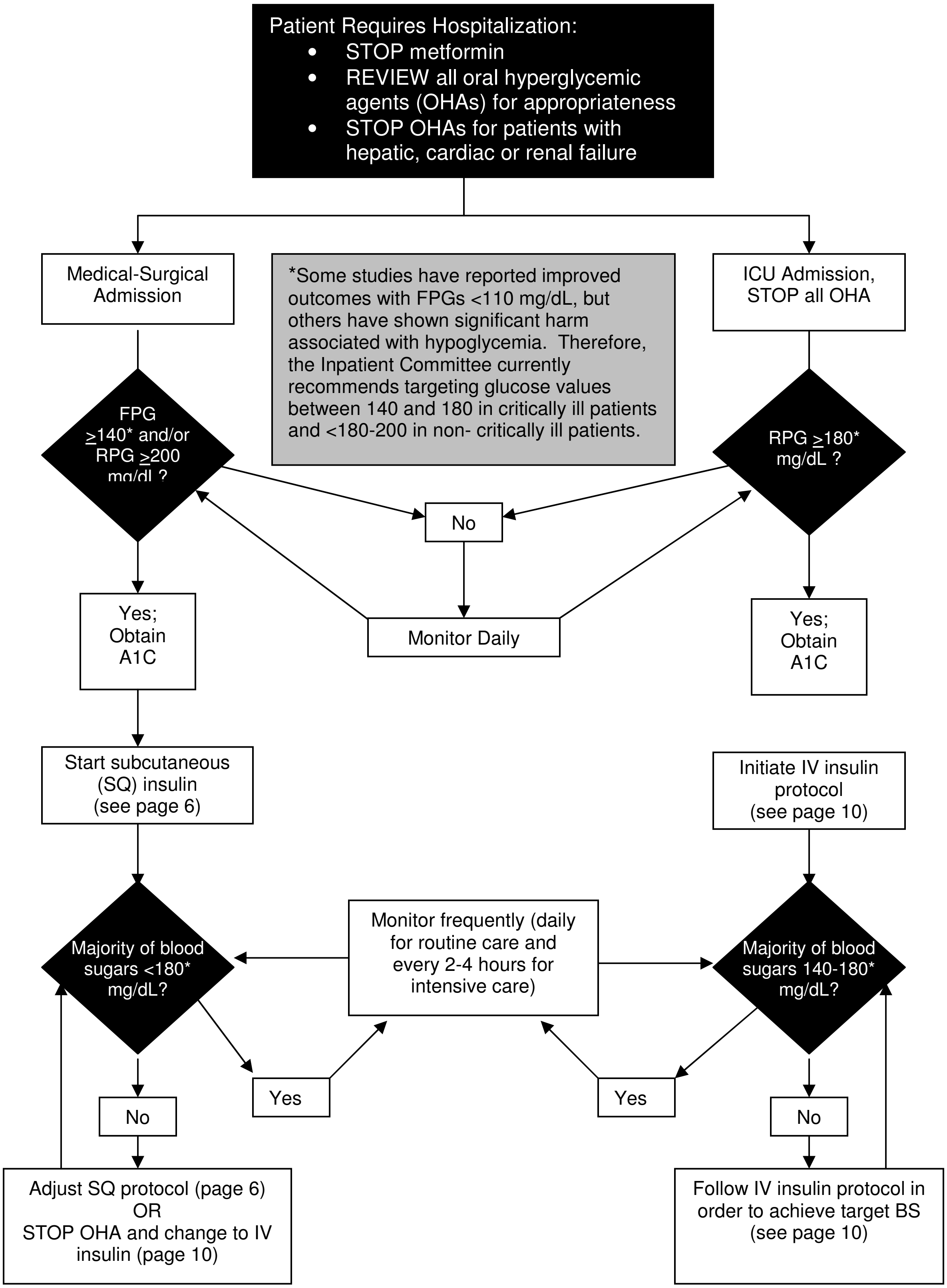
Effects of Intensive Glucose Management

Several studies have looked at how intensive management of hyperglycemia affects outcomes in hospitalized patients. The first large prospective trial, Leuven I, randomized surgical ICU patients to either tight control (target glucose 80-110 mg/dl) or to routine management. Those patients in the intensive arm were placed on IV insulin if their random glucose exceeded 110 mg/dl. The results were astounding---mortality was reduced 34% and ICU-related morbidities were similarly reduced. The same authors conducted a similar trial (Leuven II) in patients admitted to a medical ICU and used an identical treatment algorithm. In contrast to the first trial in the surgical ICU, there was no significant mortality benefit demonstrated. Two other large, multi-center trials (VISEP and GLUCOntrol) were prematurely terminated because of excessive hypoglycemia without an improvement in mortality. A meta-analysis published in 2008 reviewed 29 randomized controlled trials involving 8432 patients. The studies were stratified according to source of patients (medical or surgical) and glucose targets (<110 mg/dl or <140 mg/dl). The authors concluded that there was no mortality difference between tight control and usual care, but there was an overall decreased risk of sepsis associated with tight control. As expected, there was a significantly increased danger of hypoglycemia associated with lower target glucose values (13.7 versus 2.5%). The largest multi-center trial in intensive glucose management, the NICE-SUGAR study was recently published. In contrast to other studies, an increase in mortality (2.6%) was noted in the intensive treatment arm (target glucose 81-108 mg/dl). There were no significant differences between ICU length of stay or renal replacement requirements. Given the uncertain benefits of extremely tight targets for therapy, several national organizations (ADA, AACE, Endocrine Society) have recently recommended glucose targets of 140 to 180 mg/dl in patients admitted to intensive care units. However, currently there are few published user-friendly non-computerized protocols targeting a glucose of 140-180. Therefore, we will continue to highlight the "Yale Protocol."

Despite assumptions that insulin attains a benefit indirectly by controlling blood glucose, a growing body of literature raises the question of whether insulin may have direct beneficial effects independent of its effect on blood glucose. Results of a large study of intensive insulin infusion therapy in an intensive care unit, suggest a general anti-inflammatory action of insulin. Similar observations have been repeatedly made in smaller trials. These provocative data hint that insulin therapy in the inpatient setting has significant potential for benefit. Because of the numerous contraindications to the use of oral hypoglycemic agents in the hospital, insulin is the clear choice for glucose control in the inpatient setting.

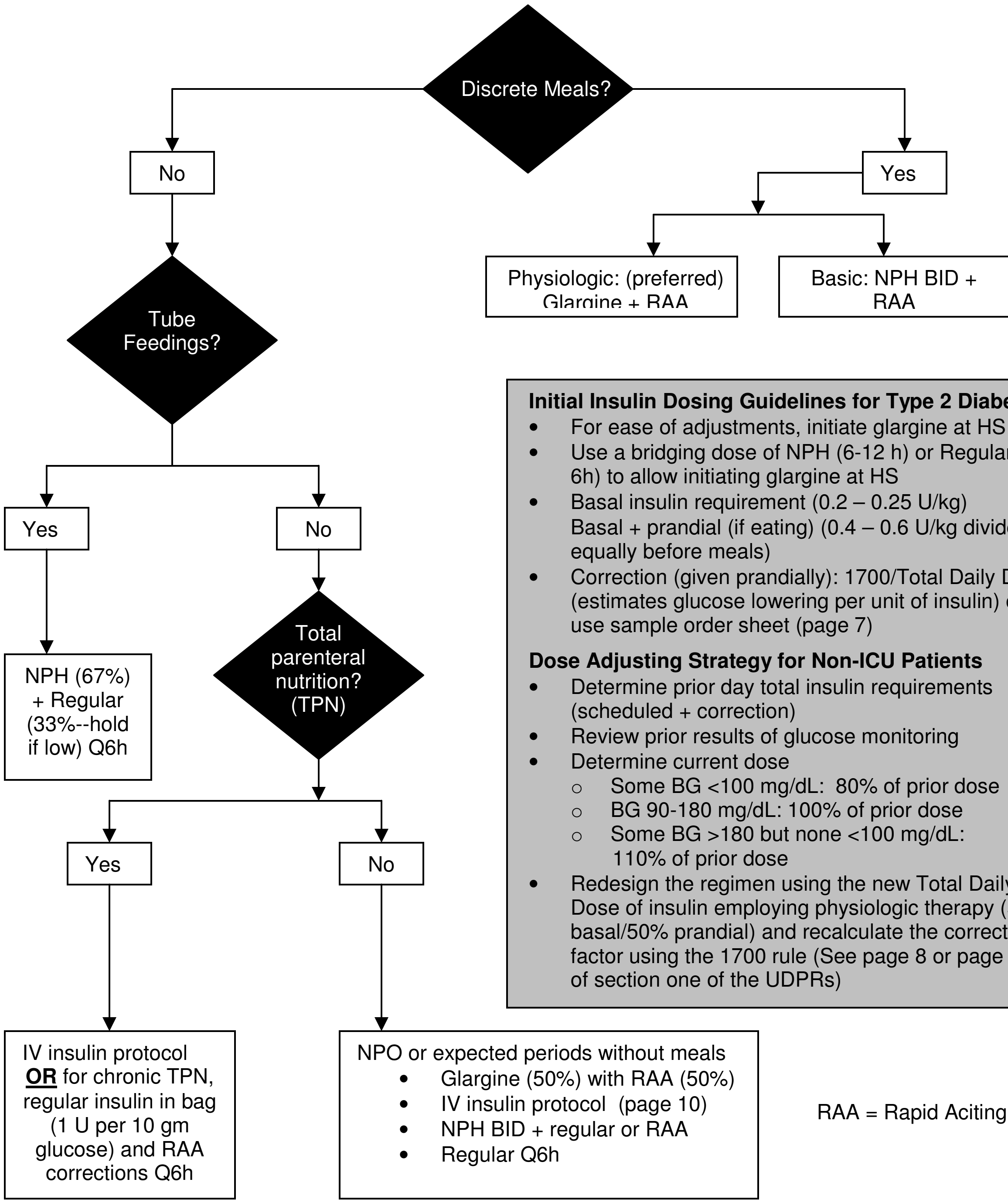
The information and algorithms that follow in this section are based on the best available published opinion and represent the current understanding of these issues. In the absence of definitive data, the committee based some of its recommendations on its own consensus opinions.

INITIAL HYPERGLYCEMIA EVALUATION



SUBCUTANEOUS INSULIN PROTOCOL

- Please keep in mind that not every contingency can be anticipated and an individual's response cannot be predicted. Edema and hypotension may alter SQ insulin absorption kinetics resulting in unexpected or cumulative effects.
- The use of "sliding scale" insulin therapy has been associated with a higher incidence of adverse metabolic outcomes and should be abandoned.
- Inpatient insulin regimens should be designed using the basal-bolus concept. These physiological regimens consist of scheduled therapy (basal insulin and planned meal-related bolus insulin) and correction therapy to address deviations in glycemic control. The typical inpatient regimen is approximately 85% scheduled therapy and 15% correction therapy.



Initial Insulin Dosing Guidelines for Type 2 Diabetes

- For ease of adjustments, initiate glargine at HS
- Use a bridging dose of NPH (6-12 h) or Regular (4-6h) to allow initiating glargine at HS
- Basal insulin requirement (0.2 – 0.25 U/kg)
  Basal + prandial (if eating) (0.4 – 0.6 U/kg divided equally before meals)
- Correction (given prandially): 1700/Total Daily Dose (estimates glucose lowering per unit of insulin) or use sample order sheet (page 7)

Dose Adjusting Strategy for Non-ICU Patients

- Determine prior day total insulin requirements (scheduled + correction)
- Review prior results of glucose monitoring
- Determine current dose
  - Some BG <100 mg/dL: 80% of prior dose
  - BG 90-180 mg/dL: 100% of prior dose
  - Some BG >180 but none <100 mg/dL: 110% of prior dose
- Redesign the regimen using the new Total Daily Dose of insulin employing physiologic therapy (50% basal/50% prandial) and recalculate the correction factor using the 1700 rule (See page 8 or page 11 of section one of the UDPRs)

SAMPLE ORDER SHEET

1. Check Blood glucose (BG)

☐ Before meals and at bedtime

☐ Every 6 hours (Patients who are NPO or getting tube feeds)

☐ Other

2. Scheduled Insulin

Insulin	Breakfast	Lunch	Dinner	Bedtime
Basal Insulin	Give ______ units ☐ glargine (Lantus) ☐ NPH	→ → **OR**	Give _____ units → → → ☐ NPH → **OR** →	Give _____ units ☐ glargine (lantus) ☐ NPH
Prandial Insulin	Give _____ units ☐ Lispro (Humalog) ☐ Aspart (Novolog) ☐ Glulisine (Apidra) ☐ Regular	Give _____ units ☐ Lispro (Humlog) ☐ Aspart (Novolog) ☐ Glulisine (Apidra) ☐ Regular	Give _____ units ☐ Lispro (Humlog) ☐ Aspart (Novolog) ☐ Glulisine (Apidra) ☐ Regular	

3. Correction Insulin Algorithm (choose an insulin and dose)

☐ Lispro (Humalog) ☐ Aspart (NovoLog) ☐ Glulisine (Apidra) ☐ Regular

- Add 1 unit for each _____ mg/dL above the preprandial target of ____ mg/dL
- Subtract 1 unit from the scheduled prandial bolus for each ______ mg/dL below the target of _____ mg/dL.
- Overnight or HS correction is one-half of the daytime correction dose.
- Apply hypoglycemic protocol for a BG < 60 mg/dl

4. Hypoglycemia protocol

A. For patients who can take PO, give 20g of fast acting carbohydrate: e.g. 6 oz fruit juice or regular soda; 12 oz low fat milk

B. If patient cannot take PO, give 25 cc of D50 IV push

C. If IV access is not available, give 1mg glucagon IM

D. Check blood glucose (BG) q15 minutes and repeat until BG >100

E. Notify provider when BG is >100 to determine if dose adjustment of scheduled insulin is warranted

Transition from Intravenous (IV) to Subcutaneous (SQ) Insulin Protocol

Plan SQ regimen in terms of basal and bolus (scheduled insulin) and correction doses (given in conjunction with meal-related bolus). In order to determine an appropriate starting dose of subcutaneous insulin, it is crucial to differentiate whether the IV insulin infusion is simply covering basal insulin requirements or if it has been used to cover nutritional needs as well.

Example 1 - IV Insulin Covers Only Basal Insulin Requirements:
If the IV infusion is simply covering basal insulin needs, use 80% of the 24 hour requirement and give it as glargine and add prandial insulin as the patient's appetite improves. Estimate **prandial insulin requirements** by dividing the number of units of the glargine dose by 3 and administering this amount of rapid acting analog (RRA) with each meal. **Correction doses** (estimation of the amount of glucose lowering per unit of insulin) are calculated as 1700/TDD (total daily dose) and are administered with meals based upon target glucose values. **(See 1700 Rule – UDPR section 1, page 13)**

Example 1

Patient is NPO, has received 2 U/h IV insulin for the past 6 hours, glucose values are stable

1. Calculate basal insulin requirements: **2U/h x 24 hours = 48 U**
   48 U x 80% = 38 U basal SQ insulin
2. Calculate prandial insulin requirements: **38/3 ~ 13 U of prandial insulin with meals**
3. Calculate correction dose: **Tally total daily dose (TDD) 38 U + 38 U = 76 U**
   1700/76 = 22 (round to a convenient number like 25)
   - 1 U is expected to lower BG ~25 mg/dL given prandially as correction dose
4. Suggested regimen: **Basal dose = 38 U glargine given at HS**
   Prandial dose = 13 U RAA with each meal (if patient is eating normally; otherwise give lower amounts and gradually increase dose as needed)

Example 2 - IV Insulin Covers Both Basal Requirements and Nutritional Needs:
Estimate 24-hour insulin requirements (total daily insulin dose or TDD) based upon the average amount of insulin infused during the preceding 6-8 hours. This assumes stable levels of blood glucose and no pressor requirements. Use 80% of this amount as the new scheduled total daily dose (TDD) and give 50% as basal insulin (glargine preferred or NPH in 2 divided doses). The basal insulin should be administered SQ two hours prior to discontinuing the IV insulin infusion. The remaining 50% is given as a rapid acting analog (RAA), divided equally by the number of daily meals, and given prandially.

Example 2

Patient received 3 U/h IV insulin for past 8 hours, glucose values are stable at 95-105 mg/dL

1. Calculate Total Insulin Requirements: **3 U/h x 24 hours = 72 U**
2. Calculate Total Daily Insulin Dose (TDD): **72 U x 80% = 58 U (TDD)**
3. Calculate Corrections Dose: **1700/58 = 29 (1 U expected to lower BG ~30 mg/dL)**
   - Add 1 U of rapid acting analog (RAA) to scheduled prandial bolus for each ~ 30 mg/dL (rounded to a convenient value) elevation in blood glucose above pre-prandial target, for example 110 mg/dL
   - Subtract 1 U of RAA from scheduled prandial bolus for each ~30 mg/dL below preprandial target
   - Overnight corrections should be made cautiously. The committee recommends using one-half of the daytime correction dose with appropriate glycemic monitoring
4. Calculate Scheduled Insulin dose **Basal dose = 58 U x 0.5 ~ 30 U (Give HS as glargine)**
   Prandial dose = 30/3 = 10 U
   (Give as RAA with meals)

Discharge Plans

To differentiate "hospital hyperglycemia" from newly diagnosed diabetes, use the A1C obtained on admission

- A1C < 5.2% is consistent with "hospital hyperglycemia"
- A1C > 6.0% is likely consistent with a diagnosis of diabetes

INTRAVENOUS INSULIN PROTOCOL (Yale Protocol)

The clinical effectiveness of the Yale protocol is well established in the medical literature (Diabetes Care 27: 461-467, 2004). Adjustments to the infusion rate are determined from the protocol's 2 tables. The protocol is simple and easily applicable once its underlying principles are understood. In the tables below, Δ= the change (decrease or increase) in the insulin infusion rate, and 2Δ = a doubling of the change in the infusion rate.

Table 1:

BG 75-99 mg/dL	BG 100-139 mg/dL	BG 140-199 mg/dL	BG ≥ 200 mg/dL	INSTRUCTIONS
		BG ↑ by >50 mg/dL/hr	BG ↑	↑ INFUSION BY "2Δ"
	BG ↑ by >25 mg/dL/hr	BG ↑ by >1-50 mg/dL/hr *OR* BG UNCHANGED	BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	↑ INFUSION BY "Δ"
BG ↑	BG ↑ by 1-25 mg/dL/hr BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 1-50 mg/dL/hr	BG ↓ by 26-75 mg/dL/hr	NO INFUSION CHANGE
BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 26-50 mg/dL/hr	BG ↓ by 51-75 mg/dL/hr	BG ↓ by 76-100 mg/dL/hr	↓ INFUSION BY "Δ"
BG ↓ by >25 mg/dL/hr*	BG ↓ by >50 mg/dL/hr	BG ↓ by >75 mg/dL/hr	BG ↓ by >100 mg/dL/hr	HOLD X 30 MIN, THEN ↓ INFUSION BY "2Δ"

Table 2:

Current Rate (U/hr)	Δ = Rate of Change (U/hr)	2Δ = 2 x Rate Change (U/hr)
<3.0	0.5	1
3.0–6.0	1.0	2
6.5–9.5	1.5	3
10.0–14.5	2.0	4
15.0–19.5	3.0	6
20.0–24.5	4.0	8
≥ 25	≥5.0	10 (consult ordering physician)

Starting the Infusion:
Dividing the starting blood glucose by 100 and rounding to the nearest half unit determines the initial bolus and infusion rate.

Example: If the starting glucose is 255 mg/dL (255 ÷ 100 = 2.55; round to 2.5). Give 2.5 units as an IV bolus and start the insulin infusion at 2.5 units/hour

PRINCIPLE 1: The rate of the insulin infusion is affected by the difference between the current and goal glucose values. The greater the difference between the current and goal values, the greater will be the corresponding rate of insulin infusion. This principle directs the selection of the column in Table 1. The higher the current blood glucose level, the further to the right in the table is the applicable column.

Example: If the current blood glucose were 195 mg/dL, the third column would be selected.

BG 75-99 mg/dL	BG 100-139 mg/dL	BG 140-199 mg/dL	BG ≥ 200 mg/dL	INSTRUCTIONS
		BG ↑ by >50 mg/dL/hr	BG ↑	↑ INFUSION BY "2Δ"
	BG ↑ by >25 mg/dL/hr	BG ↑ by >1-50 mg/dL/hr *OR* BG UNCHANGED	BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	↑ INFUSION BY "Δ"
BG ↑	BG ↑ by 1-25 mg/dL/hr BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 1-50 mg/dL/hr	BG ↓ by 26-75 mg/dL/hr	NO INFUSION CHANGE
BG UNCHANGED *OR* BG ↓ by 1-25 mg/dL/hr	BG ↓ by 26-50 mg/dL/hr	BG ↓ by 51-75 mg/dL/hr	BG ↓ by 76-100 mg/dL/hr	↓ INFUSION BY "Δ"
BG ↓ by >25 mg/dL/hr*	BG ↓ by >50 mg/dL/hr	BG ↓ by >75 mg/dL/hr	BG ↓ by >100 mg/dL/hr	HOLD X 30 MIN, THEN ↓ INFUSION BY "2Δ"

*Corrected July, 2007

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